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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/534,191 | 05/06/2005 | Jeffrey Stonehouse | 06275-453US1 100894-1P | 9980 |
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| FISH & RICHARDSON P.C. P.O BOX 1022 MINNEAPOLIS, MN 55440-1022 | | | EXAMINER MORRIS, PATRICIA L | |
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1625

DATE MAILED: 07/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 10/534,191 | Applicant(s) STONEHOUSE, JEFFREY | |
| | Examiner Patricia L. Morris | Art Unit 1625 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 June 2006.
 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6, 13-23 is/are pending in the application.
 4a) Of the above claim(s) 13-16 and 19 is/are withdrawn from consideration.
 5) ☐ Claim(s) _____ is/are allowed.
 6) ☒ Claim(s) 1-4, 6, 17, 18 and 20-23 is/are rejected.
 7) ☐ Claim(s) _____ is/are objected to.
 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-4, 6, 17, 18 and 20-23 are under consideration in this application.

Claims 13-16 and 19 are held withdrawn from consideration as being drawn to nonelected subject matter 37 CFR 1.142(b). Claim 14 is held withdrawn from consideration because it requires an additional active ingredient which is drawn to a patentably distinct invention.

Election/Restrictions

Applicant's election without traverse of Group I, process (a) recited in claim 18 and the treatment and prophylaxis of inflammatory disease in the reply filed on June 8, 2006 is acknowledged.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 6, 17 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkinshaw et al. (WO 02/090332).

Birkinshaw et al. generically embrace the instant compounds. Note the compounds of formula (I) wherein V is S, R² is a thiazole and R¹, R³ is hydrogen.

It is believed that one having ordinary skill in the art would have found the claimed compounds prima facie obvious, since they are generically embraced by the disclosed formula; In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). See also In re Malagari, 499 F.2 1297,

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182 USPQ 549 (CCPA 1974); *In re Lemin*, 332 F.2d 839, 141 USPQ 814 (CCPA 1964); *In re Rosicky*, 276 F.2d 656, 125 USPQ 341 (CCPA 1960). The requisite motivation for arriving at the claimed compounds stems from the fact that they fall within the generic class of compounds disclosed by Birkinshaw et al. Accordingly, one having ordinary skill in the art would have been motivated to prepare any of the compounds embraced by the disclosed generic formula, including those encompassed by the claims, with the expectation that each of them would be suitable for the treatment of inflammation.

It is believed well settled that a reference may be relied upon for all that it would have reasonably conveyed to one having ordinary skill in the art. *In re Fracalossi*, 681 F.2d 792, 215 USPQ 569 (CCPA 1982); *In re Lamberti*, 545 F.2d 747, 192 USPQ 278 (CCPA 1976); *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976); *In re Susi*, *supra*.

Further, Birkinshaw et al. teach specific compounds that differ only in having V as oxygen.. Note, for example, the compound recited on page 9, line 12, therein. However, Birkinshae et al. teach the optional interchangeability of oxygen and sulfur for Z. One having ordinary skill in the art would have been motivated by the disclosure of the prior art compounds to arrive at other compounds within the claimed genus as well as at the claimed species. The motivation to make these compounds is their close structural similarities to the disclosed compound. Note that the disclosed compound have antiinflammatory activity, thus the skilled artisan would expect such structurally similar compounds to possess similar properties. While homology is considered to be present even if true “homology” is not present, such does not defeat the prima facie case of obviousness raised by the art. Attention, in

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this regard is directed to *In re Druey et al.*, 50 CCPA 1538, 319 F.2d 237, 138 USPQ 39, wherein Judge Worley, delivering the Court's opinion, stated:

that "We need not decide here whether the compounds in question are properly labeled homologues. It appears to us from the authorities cited by the solicitor and appellants the term homologue is used by chemists at times in a broad sense, and at other times a narrow or strict sense. The name used to designate the relationship between the related compound is not necessarily controlling; it is the closeness of that relationship which is indicative of the obviousness or unobviousness of the new compound." 50 CCPA 1541.

Also, as the Court stated in *In re Payne et al.*, 606 F.2d 302, 203 USPQ 245 at 255 (CCPA 1979):

"the name used to designate the relationship between related compounds is not necessarily controlling; it is the closeness of that relationship which is indicative of the obviousness or unobviousness of the new compound."

In addition, any question of why would one conceive and use the similar compounds (i.e. "motivation") is answered by the Court in *In re Gyurik et al.*, 596 F.2d 1012, 201 USPQ 552 at 557.

"In obviousness rejections based in close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the prima facie case of obviousness, rises from the expectation that compounds similar in structure will have similar properties."

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Birkinshaw et al.*

Birkinshaw et al. disclose the instant process. Note reaction variant (a) on pages 11 and 12 therein. As here, a compound of formula (II) is reacted with a leaving group in the compound of formula (III). Hence, the process is deemed to be prima facie obvious since it is expected that the reactants will behave in the same manner.

A long line of cases had that the mere use of a different starting material, whether novel or known, in a conventional process to produce the product one would expect therefrom does not render the process unobvious. *In re Surrey et al.* (CCPA 1963) 319 F2d 233, 138 USPQ 67; *In re*

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Kanter (CCPA 1968) 399 F2d 249, 158 USPQ 331; In re Larsen (CCPA 1961) 292 F2d 531, 130 USPQ 209; In re Albertson (CCPA 1964) 332 F2d 379, 141 USPQ 730; Ex parte Ryland et al. (POBA 1948) 108 USPQ 15; In re Kerkhoven (CCPA 1980) 626 F2d 846, 205 USPQ 1069.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

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The nature of the invention

The nature of the invention is drawn to the method of using NOS inhibitors compounds in the treatment and prevention of any and all unknown inflammatory diseases.

State of the Prior Art

It is known the large amounts of nitric oxide (NO) are produced at sites of inflammation through the action of inducible nitric oxide synthase (iNOS) present in both infiltrating leukocytes and activated, resident cells. However, the role of nitric oxide in inflammation remains unclear and inhibitors of nitric oxide synthase (NOS) have potent prophylactic activity in several but not all animal models of inflammatory disease. Note Evans p. 110. While there is considerable evidence that excessive NO synthesized from L-arginine by iNOS plays an important pathological role in inflammatory disease, controlling the unregulated overproduction of nitric oxide from iNOS has been a formidable task. Note Rimoldi et al. (see abstract). While NOS inhibitors are implicated in the treatment of inflammatory disease, the functional effects unequivocally associated with the inhibition of NOS have not been fully established. Note Stefanovic-Racic et al, abstract, it is stated that inhibitors of NOS are good prophylactic agents in some, but not all, animal models of rheumatoid arthritis. The art of record (for example, note Cheshire) teach that a class of compounds are recited to be selective inhibitors of (iNOS) may be useful for the treatment of inflammatory conditions.

Predictability/unpredictability of the art.

The high degree of unpredictability is well recognized in the NOS inhibitor area. Note Fletcher et al., last paragraph on page 720. Fiehl et al. states that highly potent and highly selective inhibitors of iNOS effects in specific disease conditions are not readily predictable. The

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state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e., what compounds can prevent or treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles established that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any treatment regimen on its face.

The amount of direction or guidance and the presence or absence of working examples

The specification is silent as to whether if any compound treats or reduces the risk any and all unknown inflammatory diseases such as psoriasis, eye conditions, inflammatory bowel disease, prostates inflammation, etc.

The breadth of the claims

The breadth of the claims are drawn to the treatment and reducing the risk of any and all unknown inflammatory disease.

The quantity of experimentation needed

Since the instant inflammatory diseases are general classes of disorders embracing opposing and conflicting conditions arising from diverse origins, it is impossible to use a single NOS inhibitor of the instant claims to treat all these conditions. Furthermore, in view of high degree of unpredictability in the art, the limited working examples and the fact that the breadth of the claims is not commensurate with that of any objective enablement and that the nexus between the inhibitors of NOS and the recited disorders/conditions has not been established, the quantity of experimentation needed would be undue when faced with the lack of direction and

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guidance present in the instant specification in regards to the compounds and pharmaceutical compositions.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b). Applicants are also referred to In re Wands, 858 f.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in Ex parte Foreman, 230 USPQ 546 (Bd. Of App. and Inter 1986).

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001, states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.”

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 17 fails to recite an effective amount of active ingredient. A mere trace may prove inoperable.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6, 17, 18 and 20-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8, 19-22 and 25-29 of copending Application No.10/476,958. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant compounds, their use and process of making are disclosed therein.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

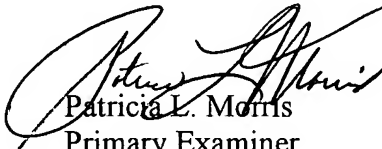
Conclusion

Claims 1-4, 6, 17, 18 and 20-23 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Patricia L. Morris
Primary Examiner
Art Unit 1625

plm
July 13, 2006